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J. Biomater. Sci. Polymer Edn, Vol. 8, No. 7, pp. 555–569 (1997)

Short review

Embolic materials for endovascular treatment of cerebral lesions

YUJI MATSUMARU,[1] AKIO HYODO,[1] TADAO NOSE,[1] TAKASHI HIRANO[2,*] and SHINICHI OHASHI[2]

[1]*Department of Neurosurgery, Institute of Clinical Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki, 305 Japan*
[2]*National Institute of Bioscience and Human Technology, 1-1 Higashi, Tsukuba, Ibaraki, 305 Japan*

Received 19 July 1996; revised 13 December 1996; accepted 14 December 1996

Abstract—Recently developed soft microcatheters can be maneuvered endovascularly into the brain, permitting treatment of lesions without conventional neurosurgery. Progress in biomaterial science has contributed significantly to the development of this new therapeutic modality termed intravascular neurosurgery or interventional neuroradiology. Although embolic materials play an important role, ideal materials have yet to be devised. Various embolic materials in clinical use are reviewed, such as cyanoacrylates, ethylene–vinyl alcohol copolymer mixtures, Ethibloc, ethanol, estrogen, poly(vinyl acetate), cellulose acetate polymer, poly(vinyl alcohol), gelatin sponges, microfibrillar collagen, surgical silk sutures, detachable balloons, and coils. The materials are reviewed in the context of treatment application for various brain lesions, such as arteriovenous malformations, cerebral aneurysms, and head and neck tumors. Further developments in biomaterial polymer science can bring about progress against brain diseases.

Key words: Embolization; embolic material; cerebral lesion; interventional neuroradiology; endovascular treatment.

1. INTRODUCTION

As biomaterial science has developed over the past decades, numerous new materials have been introduced into clinical investigation and use. Many patients who had little chance of survival two decades ago are cured by revolutionary therapies based on these materials. For treating lesions of the central nervous system (CNS), improved catheters made from new materials enable safer approaches to the brain without conventional neurosurgery. Recently, some cerebrovascular diseases such as arteriovenous malformations (AVMs) and aneurysms have been effectively treated by intravascular catheterization and embolization when conventional surgery would

*To whom correspondence should be addressed.

have carried a prohibitive complication rate [1]. Some brain tumors can be treated by intravascular therapy as a presurgical adjunct. Intravascular therapy for cerebral lesions has acquired such designations as intravascular neurosurgery, interventional neuroradiology, and surgical neuroangiography.

In 1960, Luessenhop *et al.* reported the first intravascular cerebral treatment when he embolized an AVM by injecting silastic beads into the arteries of the neck [2]. The era of selective endovascular therapy began in 1974 when Serbinenko treated a variety of neurovascular lesions using a detachable balloon technique [3]. The development of a calibrated-leak balloon catheter by Kerber allowed the first direct embolization of an AVM through the introduction of a rapidly solidifying polymer [4]. Since then endovascular treatment of brain diseases has been refined with improvements in fluoroscopic equipment, catheters, embolic agents, angiographic techniques, and understanding of neurovascular anatomy. These developments have improved not only patient survival but also their quality of life. Now further progress demands further improvements in catheters and embolic materials.

Various embolic materials have been used in endovascular treatment in the CNS, such as cyanoacrylates, ethylene–vinyl alcohol copolymer mixtures (EVAL), Ethibloc, ethanol, estrogen, poly(vinyl acetate), cellulose acetate polymer, poly(vinyl alcohol) (PVA), gelatin sponges, microfibrillar collagen, surgical silk sutures, detachable balloons, and coils. Because no ideal agent has yet been developed, a multiplicity of embolic agents has been used for a variety of indications and strategies [5]. In this paper, we review available embolic materials in the context of endovascular therapy in the CNS.

2. PRINCIPLES OF EMBOLIZATION OF CEREBRAL LESIONS

The goal of embolization is to selectively obliterate an abnormal vascular structure while preserving the blood supply to surrounding normal tissues [6]. That is accomplished with fluoroscopic equipment which can visualize the materials in the body — low-profile soft microcatheters which allow superselective catheterization into the brain — and embolic materials. In Luessenhop *et al.*'s report, the patient's neck was directly punctured, and the embolic agent was injected from that site via the carotid artery, which was remote from the target. The embolic agent was expected to be carried to the target along with the blood flow, but it could also embolize normal cerebral vessels because superselective catheterization was not achieved. Now the procedure has been refined so that in almost all cases, the microcatheter is navigated to the brain through the femoral artery, iliac artery, aorta, and carotid or vertebral artery under fluoroscopic control. In order to preserve normal tissue, the microcatheter is advanced as close to the lesion as possible. Only then is the embolic material injected through the microcatheter into the targeted lesion.

Various authors have suggested the requirement of an ideal embolic material. According to Picard *et al.* in 1977, the ideal embolic material for intravascular neurosurgery would be a solidifying liquid with an adjustable setting point: malleable when solid, stable *in vivo*, nontoxic, radiopaque, and sterile [7]. Lasjaunias *et al.* in 1987 mentioned that liquid embolic agents must be liquid at the time of injection and should solidify at the target to produce an endovascular cast of that area without passing into the venous circulation. The ideal liquid embolic agent also would be nonabsorbable, as well as intentionally nontoxically dissolvable in case of undesired location [5]. In 1995, Standard *et al.* specified that an ideal embolic agent should be nonbiodegradable, nontoxic, and nonmutagenic. It should be easily delivered through a microcatheter, be seen easily on fluoroscopy, and adhere to the walls of vessels without extravasation or recanalization [8].

No single embolic material can be used in all circumstances. The choice of embolic material depends on the anatomy and size of the target vessel, the type and position of the catheter, the desired duration of occlusion (e.g. permanent or temporary), and the specific purpose of embolization.

Embolic materials available now make up four groups; liquids, particles, coils, and balloons (Table 1). Liquid materials are used very commonly in the treatment of AVMs (Fig. 1). Some authors believe the ideal embolic material would be liquid [5, 7, 8]. Because injection through the microcatheter is easy if the viscosity is low enough, the agent will penetrate deeply into the lesions to be permanently occluded. However, there is a possibility that liquids can pass through the lesion and cause complications by occluding the venous system, especially if the lesion has significant arteriovenous shunting or includes a fistula.

Particulate materials are commonly used for preoperative embolization of AVMs and tumors (Fig. 2). Particle embolization refers to the mechanical blockage of a vessel

Table 1.
Embolic materials for endovascular treatment of cerebral lesions

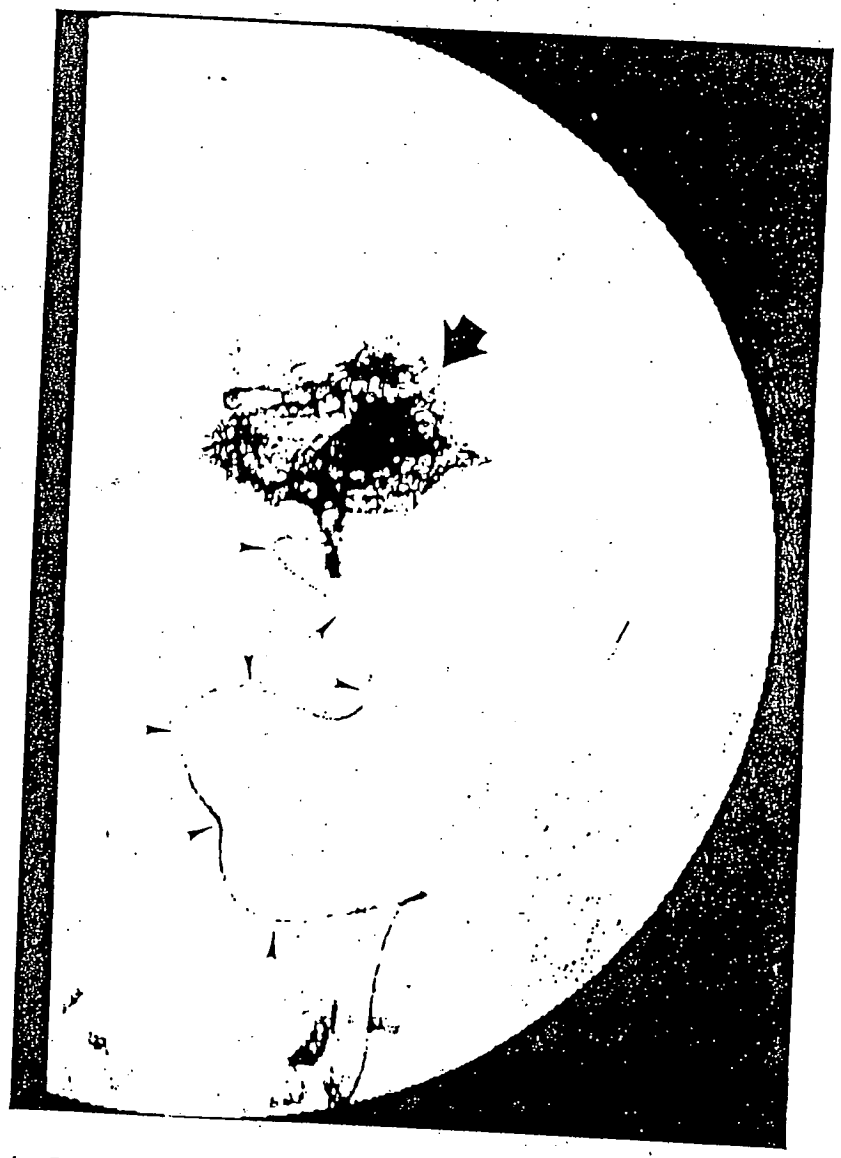
	Materials	Size of embolized vessels	Applicable diseases
Liquids	Cyanoacrylate	NF	AVM
	Ethylene–vinyl alcohol copolymer	> 80 μm	AVM
	Ethibloc	NF	AVM
	Ethanol	< 100 μm	Malignant tumor
	Estrogen	< 100 μm	AVM
	Poly(vinyl acetate)	> 100 μm	AVM
	Cellulose acetate polymer	NF	Aneurysms
Particles	Poly(vinyl alcohol)	> 100 μm	Preoperative embolization of tumors, epistaxis
	Gelfoam	50 ~ 200 μm	Preoperative embolization of tumors
	Microfibrillar collagen	25 ~ 250 μm	Preoperative embolization of tumors
	Surgical silk suture	NF	AVM
Balloons	Latex, Silicone	> 4 mm	Occlusion of large vessels
Coils	Platinum	NF	Aneurysm, occlusion of large vessels

NF: not find the description in literature.

(A)

Figure 1. (A) Angiogram of brain AVM, frontal view. A tangled mass of dilated tortuous vessels is shown (arrow). Arrow heads show the early venous filling (the shunt flow to the vein). (B) Superselective angiogram of the AVM, frontal view. A microcatheter was maneuvered into the feeding artery of the AVM (arrow heads). The AVM is shown without normal artery of the brain (arrow). Liquid embolic material is injected through this catheter.

with individual particles of uniform sizes and shapes which largely determine their occlusive properties. The large particles tend to lodge more proximally which is safer. However, the effect of large-particle emboli tends to be temporary and less effective,



(B)

Figure 1. (Continued).

because the smaller vascular bed distal to the embolization, which forms a collateral pathway, is not occluded. On the other hand, distal embolization with small particulate or liquid embolic materials tend to be very efficient and more permanent; however, the risk to normal tissues is higher [9]. In any particle embolization, recanalization can occur around the particles, because the occlusion of vessels is achieved with particles and autologous clots even if it appears as dense packing.

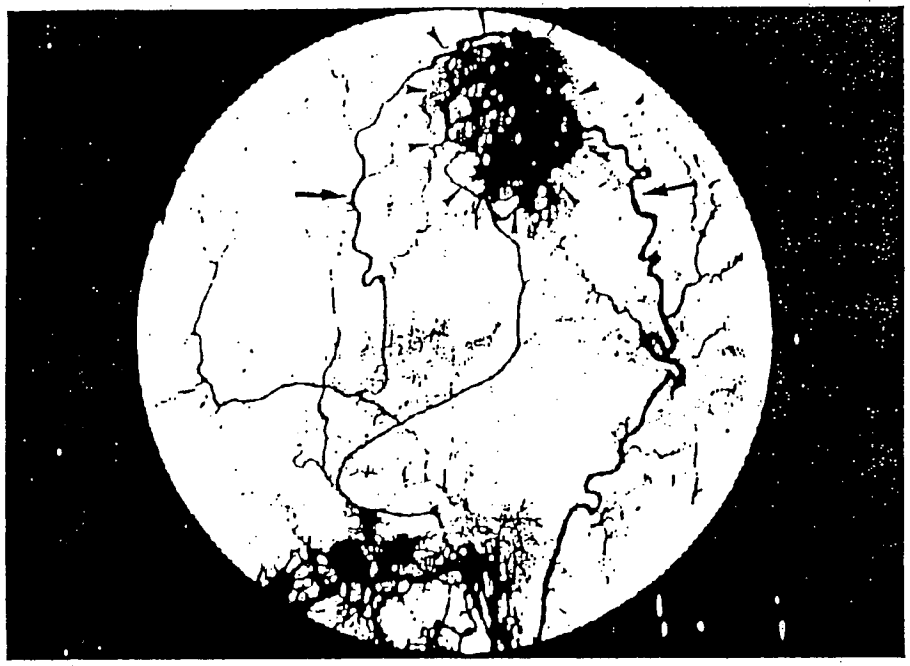


Figure 2. Angiogram of a meningioma of the brain, lateral view. The feeding artery (arrow) and tumor stein (arrow heads) are shown.

Coils for endovascular occlusion of cerebral vessels, made of platinum which is very malleable and thrombogenic, are used for the occlusion of cerebral aneurysms (Fig. 3) and for attaining more proximal occlusion of vessels than can be obtained with particles and liquids. Endovascular treatment of cerebral aneurysms with coils is epoch-making and rapidly spreading worldwide [10–12].

Balloons were once used to occlude aneurysms [13, 14], but now these are used for the most proximal occlusion of large vessels and the occlusion of fistulas lesions [15–17].

3. ENDOVASCULAR TREATMENT OF CEREBRAL LESIONS

3.1. AVMs of the brain

Arteriovenous malformations are characterized by abnormal shunting between arteries and veins in a location where capillaries would exist in the normal peripheral circulation architecture. Venous pressure and flow are diminished normally by capillaries — vessels with highest resistance. The arteries of AVMs passively enlarge over time, because high flow volume results from the abnormally low peripheral resistance of the arteriovenous shunt. The veins draining the shunt undergo progressive enlargement with increasing tortuousness as a result of the high flow volume and sustained

Figure 3. Angiogram of cerebral aneurysm, oblique view. A spherical dilatation of artery shown (arrow).

increased pressure. The gross appearance of an AVM is that of a tangled mass of dilated tortuous vessels (Fig. 1A).

The first symptom of an AVM is usually either a hemorrhage or a seizure. Surgical extirpation, when possible, was the only curative treatment until recently when embolization began to grow in importance. Embolization of brain AVMs is undertaken to facilitate surgical removal or radiation therapy, but also as a primary treatment. The microcatheter is placed within an arterial feeder of the AVM (Fig. 1B). The em-

bolic agent of choice for preoperative embolization is particulate matter, such as PVA. Surgical silk sutures are sometimes used additionally to obliterate larger fistulas, and embolization is completed with PVA.

Cyanoacrylates are used to embolize AVMs when more permanent obliteration is desired. This material is used as the sole treatment and also is used to reduce the size of the AVM so that radiation therapy can be more effective [6]. EVAL, poly(vinyl acetate), estrogen, and Ethibloc are liquids that have been used for the embolization of AVMs as a liquid material.

3.2. Cerebral aneurysms

Cerebral aneurysms are abnormal spherical dilatations of arteries with weak walls prone to rupture (Fig. 3), causing subarachnoid hemorrhage. Their usual treatment consists of surgical isolation of the aneurysm from the circulation using a specially developed clip.

Endovascular occlusion of intracranial aneurysms is an alternative therapy for aneurysms that are difficult to manage surgically [1]. Extremely soft platinum microcoils have been developed for the embolization of aneurysms [10, 11] (Fig. 3), and favorable results have been reported [12]. This new field of endovascular treatment is now rapidly developing.

3.3. Head and neck tumors

Embolization of the arterial supply of vascular tumors of the head and neck region has emerged as an accepted preoperative adjunct therapy [18]. The goal of embolization is to make surgery safer and to allow for more complete excision by devasculizing the lesion with embolic material. This embolization is best accomplished with PVA. Surgery should be done within 7–10 days because further delay allows recanalization [6].

4. EMBOLIC MATERIALS

4.1. Liquids

4.1.1. Cyanoacrylates. Cyanoacrylates are the most common currently used liquid embolic material [19, 20]. In the past, isobutyl-2-cyanoacrylate (IBCA) has been used [21–29]. *N*-Butyl-2-cyanoacrylate (NBCA) (Avacryl; Tri-Point Medical, Racegia, NC, USA and Histoacryl; B. Braun, Melsungen, Germany) has taken the place of IBCA, because of questions of mutagenicity from IBCA [5, 30–34]. NBCA is a vinyl monomer of the alkyl-2-cyanoacrylates which was developed as a tissue adhesive. When it is injected into vessels through microcatheters, it polymerizes on contact with blood which is an ionic solution. It then becomes solid and occludes vessels. Polimerization time of cyanoacrylates can be prolonged by the addition of iophendylate (Pantopaque; Lafayette Pharmacal, Lafayette, IN, USA),

glacial acetic acid, poly(phosphoric acid), octanoic acid, monoalkyl phosphoric acid ester, etho-10-(iodophenyl), nitric acid (vapor phase), and sulfur dioxide (vapor phase) [5, 20, 28, 31, 35, 36]. Tantalum powder or bismuth powder is added to the solution for opacification under fluoroscopy.

NBCA is an effective embolic material, especially in brain AVMs. It is able to permeate far distally to reach very small vessels, and its embolic occlusive effect is permanent [6, 9]. However, extensive training and experience is required for their use because adhesiveness may inadvertently bind catheters to vessel walls [9].

4.1.2. Ethylene–vinyl alcohol copolymer (EVAL) mixtures. This material consists of ethylene–vinyl alcohol copolymer and metrizamide powder, which is a contrast material for opacification, dissolved in dimethyl sulfoxide (DMSO). Upon contact with blood, DMSO rapidly diffuses into the circulation, and an EVAL elastic soft sponge is formed [37, 38]. This material was used for the embolization of AVMs [39], but DMSO, a polar organic solvent, damages the endothelium of the embolized vessels and dissolves the polyurethane commonly used in microcatheters [40].

4.1.3. Ethibloc. Ethibloc (Ethicon, Hamburg, Germany) is an ethanolic (60%) solution of 210 mg zein (corn protein)/ml ethanol, 162 mg sodium amidotrizoate/ml ethanol, 145 mg oleum papaveris/ml ethanol, and 6 mg propylenglycol/ml ethanol. As the alcohol dissolves in aqueous media, zein precipitates and forms a cast with a consistency resembling chewing gum [41–45]. Injection through a microcatheter is not smooth, because of its high viscosity [9].

4.1.4. Ethanol. Ethanol has a cytotoxic effect on target tissues and a sclerosing effect on the arterial wall, leading to intimal denudation, denaturation of vessel wall proteins, and thrombosis [46–50]. Ethanol does not produce the immediate devascularization or mechanical blockage that can be obtained with other liquid or particle embolic materials. However, it causes tissue necrosis due to cytotoxicity. It is suitable for the embolization of malignant tumors [6, 50].

4.1.5. Estrogen. Conjugated estrogen dissolved in 25% ethanol is used as a liquid embolic material [51–53]. Infusion of estrogen–ethanol causes local spherocytosis of red blood cells and severe rapid degeneration of endothelial cells, followed by injury to underlying muscle cells and fibroblasts. It induces immediate occlusion of small vessels (<20 μm), and then progressive obstruction of larger ones (>200–300 μm) within a few days. Estrogen–ethanol causes similar embolization to absolute ethanol, but no direct damage to perivascular tissue [54].

4.1.6. Poly(vinyl acetate). Poly(vinyl acetate) dissolved in ethanol becomes gelatinous on contact with an aqueous environment and occludes vessels [55]. This material is used with estrogen to augment the embolization effect [52, 53].

4.1.7. Cellulose acetate polymer. Cellulose acetate polymer (CAP) is the only liquid embolic material developed for the treatment of aneurysms [56]. CAP is mixed with bismuth trioxide for the opacification under fluoroscopy and dissolved in DMSO. CAP is injected directly into the aneurysm through a microcatheter previously manipulated into it. On contact with blood, DMSO diffuses and CAP solidifies, ballooning as it is injected slowly into the aneurysm and, therefore, occluding it.

4.2. Particles

4.2.1. Poly(vinyl alcohol) (PVA). PVA has seen long used as a biocompatible material [57–59], being the most commonly used particulate embolic agent [9, 60, 61]. This material is supplied as dry particles of a size chosen based on the diameter of target vessels. Embolization catheters accept up to 700 μm particles. Although PVA particles are not biodegradable, the vascular occlusion produced with PVA may be followed by some irregular recanalization [5]. Therefore, these particles are suitable for the preoperative devascularization of tumors, AVMs, and the hemostasis of epistaxis — situations where permanent occlusion is not necessary [6, 62–65].

4.2.2. Gelatin sponges (Gelfoam). Gelatin sponge (Gelfoam; Upjohn, Fort Lee, NJ, USA) was first used to control hemorrhage during neurosurgical procedures [66] and has been adapted as an embolic material for endovascular treatment [67, 68]. It is commercially available as a powder (40–60 μm particle), and as sheets or cubes from which pieces of varying size easily can be cut. Gelfoam powder is an excellent temporary occlusive agent for small vessel devascularization, and in hypervascular tumors prior to surgical removal [6, 69, 70]. Gelfoam sponge can be cut into large pledgets (1 × 2–3 mm), which can be safely used to block large arteries to prevent unwanted distal embolization with either particulate or liquid embolic agents [6]. Vascular occlusion accomplished with Gelfoam is temporary, and recanalization occurs about 7–21 days after embolization [71, 72].

4.2.3. Microfibrillar collagen (Avitene). Avitene (Medchem Product, Woburn, MA, USA) was developed as an intra-operative hemostatic agent. It is a microcrystalline polymer prepared from purified bovine collagen. Injected Avitene occludes small vascular beds, since particle size ranges from 75 to 150 μm [73, 74]. Recanalization occurs in arteries occluded with Avitene.

4.2.4. Surgical silk sutures. Surgical sutures can be used as an embolic material when cut in to 3–10 mm lengths. Silk sutures incite an intense local inflammatory reaction [75, 76], which can occlude fistulas in AVMs where particulates such as PVA would pass through [6].

4.3. Detachable balloons

Detachable balloons, originally developed by Serbinenko *et al.* in Russia for the treatment of aneurysms [3, 77], now are used for major vessel occlusion, such as

internal carotid or vertebral arteries and traumatic large fistulas. Balloons are mounted at the distal end of a microcatheter. When the balloon reaches the lesion, it is filled with a solidifying agent or contrast material, and detached from the microcatheter. Balloons are available with self-sealing valves ensuring that when the microcatheter is withdrawn the balloon remains inflated. The two types of balloons currently available are latex (Ingeor Laboratories, Paris, France) and silicone (Interventional Therapeutics, South San Francisco, CA, USA). Latex is an essentially impermeable membrane, while silicone is semipermeable. Therefore silicone balloons must be inflated with an isomolar solution (such as metrizamide, 170–200 mg of iodine per milliliter of solution, or with isomolar nonionic angiographic contrast medium) [78, 79]. Silicone balloons have a higher expansion coefficient and are softer and less rigid than latex balloons [9].

4.4. Coils

Stainless steel coils have long been used for peripheral embolization purposes. They are very thrombogenic owing to an attached dacron fiber, facilitating occlusion [80, 81]. However, they are too stiff for cerebral vessels. Different shapes for platinum microcoils, which are softer than stainless coils, were developed for endovascular occlusion of major vessels and aneurysms (Fig. 4). Recently, Guglielmi *et al.* developed a detachable platinum coil (GDC coils: Target therapeutics, CA, USA) for the treatment

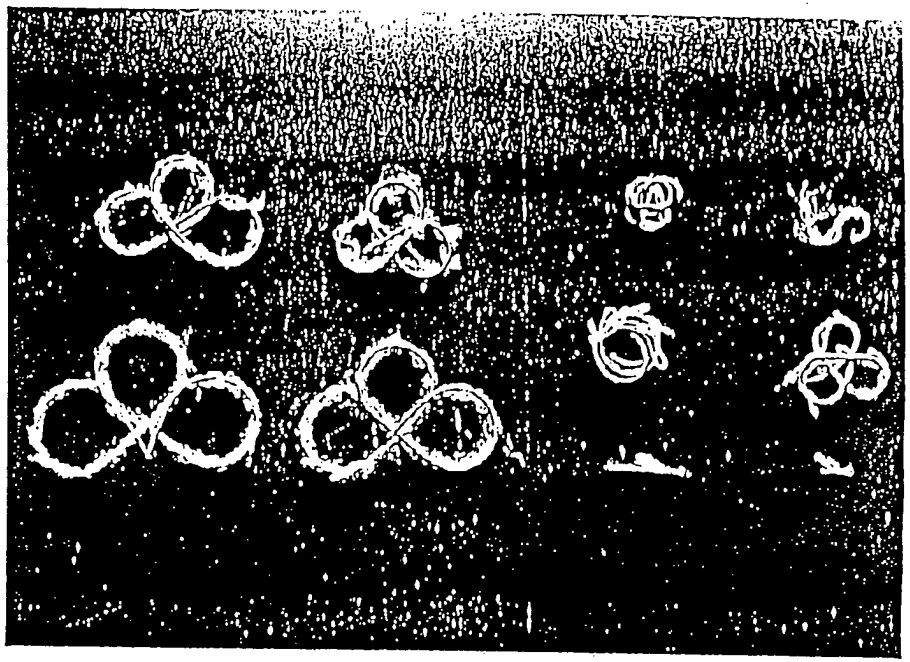


Figure 4. Fibered platinum coils (Target therapeutics, CA, USA). There are some variety of shapes. Dacron fibers are attached to facilitate the thrombosis.

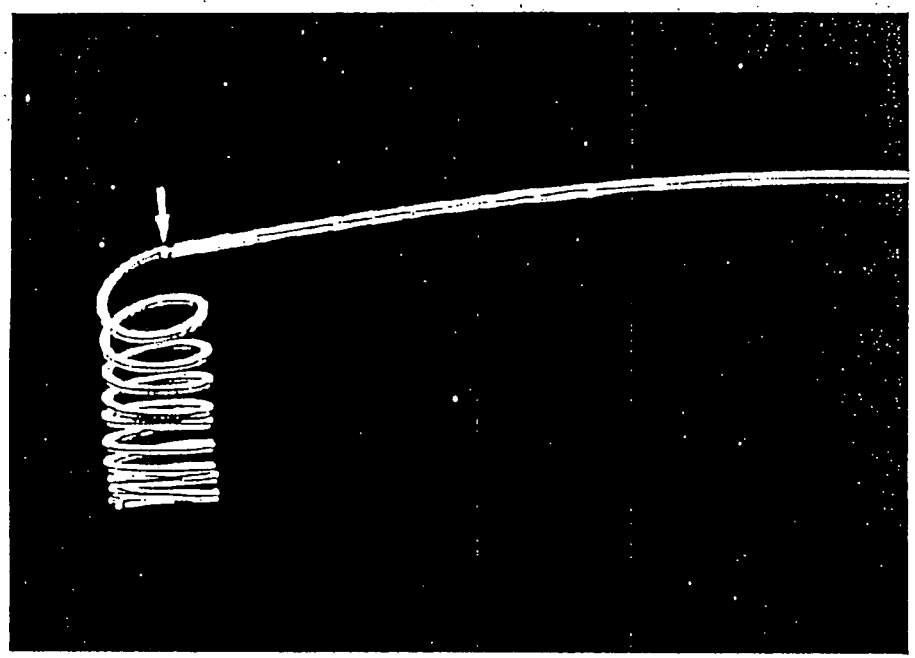


Figure 5. Electrolytic detachable coils (GDC coil: Target therapeutics, CA, USA). This coil is manufactured from a platinum alloy which pemits it to conform to the often irregular shape of saccular aneurysms. This coil is attached to a stainless steel delivery wire which permits repositioning and selective placement of the coil within an aneurysm. The coil can be detached by electrolytic process at the connecting part (arrow).

of cerebral aneurysms (Fig. 5). This coil is very soft, and has a great variety of size and length to fit aneurysms. This coil is attached to a stainless steel delivery wire which permits repositioning and selective placement of the coil within an aneurysm, and is detached by direct current by an electrolytic process [10, 11].

5. CONCLUSION AND PROSPECTS

For the treatment of AVMs, NBCA presently seems to be the most effective embolic material. It's adhesion to the vessel walls provides positive occlusion, but adhesion to the catheter threatens serious problems. The ideal material would adhere selectively to the vessel wall without adhesion to the catheter. In practice, excessive or wrong embolization sometimes occurs, so potential reversibile recanalization is desired in an ideal material.

For the treatment of aneurysms, the detachable platinum coil is suitable but very expensive for large and giant aneurysms, which require many coils. A polymeric material which can take place of costly platinum coils is desired.

For the treatment of benign tumors, PVA is suitable for preparative devascularization. The treatment of malignat tumors is still challenging. Combinations of chemotherapy and embolization, such as controllable release of antitumor drug from the embolic material, is a possible future therapeutic modality.

REFERENCES

1. F. Viñuela, J. Dion, P. Lylyk and G. R. Duckwiler, in: *Neurosurgery Update 2*, R. H. Wilkins and S. S. Rengachary (Eds), p. 142. McGraw-Hill, New York (1991).
2. A. J. Luessenhop and W. T. Spence, *J. Am. Med. Assoc.* 172, 1153 (1960).
3. S. A. Serbinenko, *J. Neurosurg.* 41, 125 (1974).
4. C. Kerber, *Radiology* 120, 547 (1976).
5. P. Lasjaunias and A. Berenstein, *Surgical Neuroangiography. 2. Endovascular Treatment of Cranio-facial Lesions*. Springer-Verlag, Berlin/Heidelberg (1987).
6. J. M. Eskridge, *Neuroradiology* 172, 991 (1989).
7. L. Picard, J. Even, J. Bertrand and E. Floquent, *J. Neuroradiol.* 4, 385 (1977).
8. S. C. Standard and L. N. Hopkins, in: *Neurosurgical Topics: Endovascular Neurological Intervention*, R. J. Maciunas (Ed.), p. 1. American Association of Neurological Surgeons, Park Ridge, IL (1995).
9. J. E. Dion, in: *Interventional Neuroradiology. Endovascular Therapy of the Central Nervous System*, V. V. Halbach, F. Viñuela and J. E. Dion (Eds), p. 1. Rawen Press, New York (1992).
10. G. Guglielmi, F. Viñuela, J. Dion and G. Duckwiler, *J. Neurosurg.* 75, 1 (1991).
11. G. Guglielmi, F. Viñuela, J. Dion and G. Duckwiler, *J. Neurosurg.* 75, 8 (1991).
12. G. Guglielmi, F. Viñuela, G. Duckwiler, J. Dion, P. Lylyk, A. Berenstein, C. Strother, V. Graves, V. Halback, D. Nichols, N. Hopkins, R. Ferguson and I. Sepetka, *J. Neurosurg.* 77, 515 (1992).
13. R. T. Higashida, G. B. Hieshima, V. V. Halbach, K. Goto, B. Dormandy, J. Bell, L. Cahan and J. R. Bentson, *Acta. Radiol. Suppl.* 369, 594 (1986).
14. W. Taki, H. Handa, S. Yamagata, M. Ishikawa, H. Iwata and Y. Ikada, *Surg. Neurol.* 13, 140 (1980).
15. G. Debrun, A. Fox and C. Drake, *Am. J. Neuroradiol.* 2, 167 (1981).
16. A. Berenstein, J. Ransohoff, M. Kupersmith, E. Flamm and D. Graeb, *Surg. Neurol.* 21, 3 (1984).
17. A. J. Fox, F. Viñuela, D. M. Pelz, S. J. Peerless, G. G. Ferguson, C. G. Drake and G. Debrun, *J. Neurosurg.* 66, 40 (1987).
18. V. V. Halbach, G. B. Hieshima, R. T. Higashida and C. F. Dowd, in: *Interventional Neuroradiology: Endovascular Therapy of the Central Nervous System.*, F. Viñuela, V. V. Halbach and J. Dion (Eds), p. 17. Raven Press, New York (1992).
19. G. Debrun, F. Viñuela, A. Fox and C. G. Drake, *J. Neurosurg.* 56, 615 (1982).
20. L. D. Cromwell and C. W. Kerber, *Am. J. Roentgenol.* 132, 799 (1979).
21. C. Kerber, *Invest. Radiol.* 10, 536 (1975).
22. F. Viñuela, A. J. Fox, G. Debrun, C. G. Debrun, S. J. Peerles and J. P. Givin, *Am. J. Neuroradiol.* 4, 1233 (1983).
23. P. M. Klara, E. D. George, D. E. McDonnel and P. H. Pevsner, *J. Neurosurg.* 63, 421 (1985).
24. F. Viñuela, A. J. Fox, G. Debrun and D. Pelz, *Am. J. Neuroradiol.* 5, 765 (1984).
25. D. M. Pelz, A. J. Fox, F. Viñuela, C. C. Drake and G. G. Ferguson, *Am. J. Neuroradiol.* 9, 757 (1988).
26. F. Viñuela, G. M. Debrun, A. J. Fox, J. P. Girvin and S. J. Peerles, *Am. J. Neuroradiol.* 4, 959 (1983).
27. F. Viñuela, A. J. Fox, D. Pelz and G. Debrun, *Am. J. Neuroradiol.* 7, 919 (1986).
28. P. H. Pevsnar, E. D. George and L. J. Doppman, *Neurosurgery* 10, 314 (1982).
29. H. V. Vinters, G. Debrun, J. C. E. Kaufmann and C. G. Drake, *J. Neurosurg.* 55, 819 (1981).
30. R. A. W. Lehman and G. J. Hayes, *Surgery* 61, 915 (1967).
31. M. F. Brothers, J. C. E. Kaufmann, A. J. Fox and J. P. Deveikis, *Am. J. Neuroradiol.* 10, 777 (1989).
32. P. A. Marck, J. E. Cummins, K. Galil, I. Schofield and G. Z. Wright, *J. Dent. Res.* 61, 288 (1982).
33. D. Samson, *J. Neurosurg.* 65, 571 (1986).
34. A. Berenstein and G. Hieshima, *J. Neurosurg.* 67, 318 (1987).
35. S. M. Spiegel, F. Viñuela, J. M. Goldwasser, A. J. Fox and D. M. Pelz, *Am. J. Neuroradiol.* 7, 109 (1986).

36. L. D. Gronwell, P. C. Freeny, C. W. Kerber, L. L. Kunz, A. B. Harris and C. W. Shaw, *Am. J. Roentgenol.* 147, 627 (1986).
37. W. Taki, Y. Yonekawa, H. Iwata, A. Uno, K. Yamashita and H. Amemiya, *Am. J. Neuroradiol.* 11, 163 (1990).
38. K. Yamashita, W. Taki, H. Iwata, I. Nakahara, S. Nishi, A. Sadato, K. Matsumoto and H. Kikuchi, *Am. J. Neuroradiol.* 15, 1103 (1994).
39. T. Terada, Y. Nakamura, K. Nakai, M. Tsuura, T. Nishiguchi, S. Hayashi, T. Kido, W. Taki, H. Iwata and N. Komai, *J. Neurosurg.* 75, 655 (1991).
40. J. C. Chaloupka, F. Viñuela, H. V. Vinters and J. Robert, *Am. J. Neuroradiol.* 15, 1107 (1994).
41. J. M. Dubois, G. H. Sebag, Y. D. Prost, D. Teillac, B. Charetien and F. O. Brunelle, *Radiology* 180, 195 (1991).
42. G. W. Kauffmann, J. Rassweiler, G. Richter, K. H. Hauenstein, R. Rohrbach and H. Friedburg, *Am. J. Roentgenol.* 137, 1163 (1981).
43. K. C. Wright, T. Bowers, V. P. Chaung and C. C. Tsai, *Radiology* 145, 339 (1982).
44. G. Richter, J. Rassweiler, G. W. Kauffmann, W. Wenz and D. B. Crawford, *Invest. Radiol.* 19, 36 (1984).
45. K. H. Barth, J. D. Strandberg, F. L. Starr, M. A. Samphilipo and J. H. Anderson, *Invest. Radiol.* 19, 517 (1984).
46. W. F. Yakes, J. M. Luethke, S. H. Parker, A. T. Stavros, K. M. Rak, K. D. Hopper, J. N. Dreisbach, D. J. Griffin, C. E. Seibert and T. E. Carter, *Radiographics* 10, 787 (1990).
47. W. F. Yakes, D. K. Haas, S. H. Parker, M. D. Gibson, K. D. Hopper, J. S. Mulligan, P. H. Pevsner, J. C. Johns and T. E. Carter, *Radiology* 170, 1059 (1989).
48. B. A. Ellman, B. J. Parkhall and P. B. Markus, *Invest. Radiol.* 19, 416 (1984).
49. P. H. Pevsner, P. Klara, J. Doppman, E. George and M. Girton, *Am. J. Neuroradiol.* 4, 388 (1983).
50. I. S. Choi, A. Berenstein and J. Scott, *Am. J. Neuroradiol.* 6, 462 (1985).
51. Y. Shimizu, Y. Nagamine, Y. Fujiwara, J. Suzuki, T. Yamamoto and Y. Iwasaki, *Surg. Neurol.* 28, 23 (1987).
52. C. C. Su, A. Takahashi, T. Yoshimoto and T. Sugawara, *Surg. Neurol.* 36, 4 (1991).
53. T. Sugawara, A. Takahashi, C. C. Su, T. Suga and T. Yoshimoto, *Neurol. Med. Chir. (Tokyo)* 33, 71 (1993).
54. T. Sugawara, A. Takahashi, C. C. Su, T. Suga, T. Yoshimoto and J. Suzuki, *Neurol. Med. Chir. (Tokyo)* 32, 59 (1992).
55. J. H. Peregrin, M. Kaspar, M. Haco, R. Vanecek and A. Belan, *Cardiovasc. Intervent. Radiol.* 7, 97 (1984).
56. K. Kinugasa, S. Mandai, Y. Terai, I. Kamata, K. Sugiu, T. Ohmoto and A. Nishimoto, *J. Neurosurg.* (1992).
57. J. Bentson and P. Crandall, *Radiology* 105, 65 (1972).
58. K. E. Hogemann, G. Gustafson and G. Bjorlin, *Acta Chir. Scand.* 121, 83 (1961).
59. S. M. Tadavarthy, L. Knight and T. W. Ovitt, *Radiology* 113, 13 (1974).
60. M. Herrera, J. Rysavy, S. Kotula, B. Rusnak, W. R. Castaneda-Zuniga and K. Amplatz, *Radiology* 144, 638 (1982).
61. C. W. Kerber, W. P. Bank and J. A. Horton, *Radiology* 130, 1193 (1978).
62. R. I. White, J. D. Standberg, J. S. Gross and K. H. Barth, *Radiology* 125, 677 (1977).
63. R. G. Quisling, J. P. Mickle, W. B. Ballinger, C. C. Carver and B. Kaplan, *Am. J. Neuroradiol.* 5, 101 (1984).
64. T. H. Lanman, N. A. Martin and H. V. Vinters, *Neuroradiology* 30, 1 (1988).
65. P. D. Purdy, D. Samson, H. H. Batjer and R. C. Risser, *Am. J. Neuroradiol.* 11, 501 (1990).
66. R. U. Light and H. R. Prentice, *J. Neurosurg.* 2, 435 (1945).
67. R. Djindjian, J. Cophignon, J. Theron, J. J. Merland and R. Houdart, *Neuroradiology* 6, 20 (1973).
68. T. J. Speakman, *J. Neurosurg.* 21, 303 (1964).
69. F. Kunstlinger, F. Brunelle, P. Chaumont and D. Doyon, *Am. J. Roentgenol.* 136, 151 (1981).
70. A. Berenstein and E. Russel, *Neuroradiology* 141, 105 (1981).
71. K. Barth, J. Strandberg and R. White, *Invest. Radiol.* 12, 273 (1977).

72. R. Gold and D. Grace, *Radiology* 116, 575 (1975).
73. S. L. Kaufman, J. Strandberg, K. H. Barth and R. I. White, Jr., *Invest. Radiol.* 13, 203 (1978).
74. A. Kumar, S. L. Kaufman, J. Patt, J. B. Posey, D. D. Maxwell and R. I. White, Jr., *Am. J. Neuroradiol.* 3, 163 (1982).
75. A. Benati, A. Beltramello, R. Colombari, A. Maschio, S. Perini, R. Da Pian, A. Pasqualin, R. Scienza, L. Rosta, E. Piovan, A. Scarpa and G. Zamboni, *Am. J. Neuroradiol.* 10, 579 (1989).
76. J. M. Eskridge and R. P. Hartling, *Am. J. Neuroradiol.* 10, 882 (1989).
77. A. P. Romodanov and V. I. Scheglov, in: *Advances and Technical Standards in Neurosurgery*, H. Krayenbuhl (Ed.), p. 25. Springer-Verlag, Vienna (1982).
78. R. T. Higashida, V. V. Halbach, C. D. Dowd, S. L. Barnwell and G. B. Hieshima, *Radiology* 178, 663 (1991).
79. R. T. Higashida, V. V. Halbach, B. Dormandy, J. D. Bell and G. B. Hieshima, *Radiology* 174, 687 (1990).
80. V. P. Chaung, S. Wallace, C. Giasnturco and C. S. Soo, *Am. J. Roentgenol.* 137, 809 (1981).
81. V. R. Rao, R. K. Mandalam, S. Joseph, V. Satija, V. K. Gupta, A. K. Gupta, S. K. Jain, M. N. Unni and A. S. Rao, *Radiology* 175, 407 (1990).